original article

Characteristics and outcomes of 974 COVID-19 patients in intensive care units in Turkey

Hülya Sungurtekin,[a] Cansu Ozgen,[a] Ulku Arslan,[a] Kemal Tolga Saracoglu,[b] Volkan Yarar,[c] Ahmet Sari,[d] Ayse Turan Civraz,[e] Ali Aydin Altunkan,[f] Hilal Ayoglu,[g] Nilgun Kavrut Ozturk,[h] Nihal Bulut Yuksel,[i] Birgul Yelken,[j] Elif Bombaci,[b] Gokhan Kilinc,[c] Damla Akman,[d] Pinar Demir,[f] Ferruh Ayoglu,[k] Fulya Ciyiltepe,[d] Ahmet Caliskan,[l] Simay Karaduman[a]

From the [a]Department of Anesthesiology and Reanimation, Pamukkale University, Denizli, Turkey; [b]Department of Anesthesiology and Reanimation, Kartal Dr. Lütfi Kırdar Şehir Hastanesi, Istanbul, Turkey; [c]Department of Anesthesiology and Reanimation, Ataturk City Hospital, Balikesir, Turkey; [d]Department of Anesthesiology and Reanimation, Istanbul Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey; [e]Department of Anesthesiology and Reanimation, Kocaeli Derince Training and Research Hospital, Kocaeli, Turkey; [f]Department of Anesthesiology and Reanimation, Mersin University Hospital, Mersin, Turkey; [g]Department of Anesthesiology and Reanimation, Zonguldak Bülent Ecevit University, Zonguldak, Turkey; [h]Department of Anesthesiology and Reanimation, Antalya Training and Research Hospital, Antalya, Turkey; [i]Department of Anesthesiology and Reanimation, Medical Faculty, Hacettepe University, Ankara, Turkey; [j]Department of Anesthesiology and Reanimation, Eskişehir Osmangazi Üniversitesi Tıp Fakültesi, Eskişehir, Turkey; [k]Department of Public Health, Zonguldak Bülent Ecevit University, Zonguldak, Turkey; [l]Department of Medical Microbiology, Pamukkale University, Denizli, Turkey

Correspondence: Prof. Hülya Sungurtekin · Department of Anesthesiology and Reanimation, Pamukkale University, 593 Sok No 13 Servergazi, Yesilkoy Denizli 20055, Turkey · hsungurtekin@yahoo.com · ORCID: https://orcid.org/0000-0002-9453-5625

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BACKGROUND: In our previous report on Turkish COVID-19 patients requiring intensive care, the 24 patients in a single ICU were elderly and mortality was high. We extended our analysis to include patients admitted to ten ICUs.

OBJECTIVES: Report the demographics, clinical features, imaging findings, comorbidities, and outcomes in COVID-19 patients.

DESIGN: Retrospective.

SETTING: Intensive care unit.

PATIENTS AND METHODS: The study includes patients with clinical and radiological confirmed or laboratory-confirmed COVID-19 infection who were admitted to ten ICUs between 15 March and 30 June 2020.

MAIN OUTCOME MEASURES: Clinical outcomes, therapies, and death during hospitalization

SAMPLE SIZE: 974, including 571 males (58%).

RESULTS: The median age (range) was 72 (21-101) years for patients who died (n=632, 64.9%) and 70 (16-99) years for patients who lived (n=432, 35.2%) (*P*<.001). APACHE scores, and SOFA scores were higher in patients who died than in those who survived (*P*<.001, both comparisons). Respiratory failure was the most common cause of hospitalization (82.5%), and respiratory failure on admission was associated with death (*P*=.013). Most (n=719, 73.8%) underwent invasive mechanical ventilation therapy.

CONCLUSIONS: The majority of patients admitted to the ICU with a diagnosis of COVID-19 require respiratory support.

LIMITATIONS: Although the Turkish Ministry of Health made recommendations for the treatment of COVID-19 patients, patient management may not have been identical in all ten units.

CONFLICT OF INTEREST: None.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China, and has spread worldwide, infecting millions of people since December 2019. Coronavirus disease 2019 (COVID-19), has various clinical manifestations, ranging from no symptoms to severe acute respiratory failure.[1,2] To combat the disease in Turkey, the COVID-19 Science Board was created on 10 January 2020 by the Ministry of Health. On 3 February, it was announced that it would stop all flights from China to Turkey. The first COVID-19 case in Turkey was detected on 11 March 2020, and the diagnosis was made by investigating the cause of symptoms of high fever and cough. The first death due to coronavirus disease in the country occurred on 17 March 2020.[3]

Collaboration at the local, national, and international levels with a focus on high-quality research, sharing of data and resources, and clinical practice will be crucial to the success of the management of COVID-19.[4] Little information is available on the characteristics and outcomes of Turkish patients with COVID-19 requiring intensive care. We previously published COVID-19 patients hospitalized in the intensive care units of our hospital in a small group of patients. In that article, we showed that in a few patients, COVID-19 is seen mostly in the elderly and those with comorbidities, and the mortality rate is high.[5] The aim of this study was to report the demographics, clinical features, imaging findings, comorbidities, and outcomes in COVID-19 patients in the ICUs of ten different hospitals in Turkey.

PATIENTS AND METHODS

In this retrospective cohort study of patients in ten ICUs in Turkey, we selected all sequential patients older than 18 years of age with laboratory-confirmed COVID-19 infection or clinical-radiological confirmed COVID-19 infection admitted to the participating ICUs between 15 March 2020 and 30 June 2020. Criteria for admission to the ICU included at least one pneumonia symptom with a breath rate >30/mins, severe respiratory distress with oxygen saturation (SpO_2) in room air below 90%, presence of sepsis, septic shock, acute respiratory distress syndrome (ARDS), and severe viral pneumonia with life-threatening conditions such as acute thrombosis. Laboratory confirmation of SARS-Cov-2 was defined as a positive result by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay from a specimen collected on a nasopharyngeal swab or endotracheal aspirate.[3] Patient data were obtained from electronic data on hospital computers. An intensivist recorded the data on a daily basis. The study was approved by the local ethics committee of Pamukkale University, Medical School, and the ethics committee of the Turkish Ministry of Health (#60116787-020/28387). Informed consent was waived because of the retrospective design of the study, and the researchers analyzed the anonymized data.

Data collection

Patient information collected at ICU admission included age, sex, smoking history, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, recent exposure and travel history, date of the first symptom, clinical symptoms or signs, laboratory findings and comorbidities, ventilator therapy and parameters, and dates of the hospital and ICU admission. Laboratory findings included a complete blood count, coagulation testing, D-dimer, blood chemical analysis, C-reactive protein, procalcitonin, and assessment of liver and renal function. Invasive mechanical ventilation parameters, such as the level of positive end-expiratory pressure (PEEP), fraction of inspired oxygen (FiO_2), plateau pressure, compliance, and noninvasive mechanical ventilation parameters, were also recorded during ICU hospitalization. Radiologic imaging such as chest radiography and/or CT was performed on day 1 as needed. Arterial blood gas analysis was performed depending on the patient's clinical condition. ARDS, sepsis, and septic shock were defined according to the guidelines.[6,7] The Turkish Ministry of Health made recommendations for the treatment of COVID-19 patients, and the evaluation of all available evidence and ongoing clinical trial protocols have been developed. This recommendation was prepared by the scientific committee of the Turkey Ministry of Health. Patients were treated according to these recommendations and available literature.[9] Therapies of the patients (drug, renal replacement therapy, mesenchymal stem cell, prone positioning, etc.) were documented daily. Informed consent forms were obtained from the patients' relatives for the use of drugs without a labeled indication drugs and methods, and permission was obtained from the Ministry of Health. Microbial cultures from tracheal aspirate, blood, and urine were collected at admission and as needed. For SARS-CoV-2, samples were evaluated in the General Office of Public Health Microbiology Reference Laboratory and laboratories in the specified provinces. RT-PCR assays (COVID-19 RT-qPCR, Bio-Speedy) were performed according to the protocol approved by the WHO in this laboratory.[8] Patient discharge status (dead or alive) and length of stay in the ICU were entered into the data form.

Statistical analysis

Data were compared between survivors and non-survivors. Statistical evaluations were performed using the IBM SPSS for Windows 19 software IBM SPSS (Armonk, New York, United States: IBM Corp) version. Descriptive statistics are summarized as counts, percentages and mean and standard deviation (SD). The chi-square test and independent samples t-test were used for compar-

Table 1. Ten intensive care unit patients admitted from 15 March and 30 June 2020.

	Number of patients	ICU beds	Attending physicians	Residents	Nurses
Lutfu Kırdar Training and Research Hospital, İstanbul	301 (30.9)	70	12	12	32
Balıkesir Atatürk City Hospital, Balıkesir	200 (20.5)	51	2	0	74
Haydarpaşa Numune Training and Research Hospital, İstanbul	110 (11.3)	21	7	5	42
Health and Science University Derince Training and Research Hospital, Kocaeli	96 (9.9)	24	4	4	22
Pamukkale University Medical Faculty, Denizli,	83 (8.5)	50	4	6	28
Mersin University Medical Faculty, Mersin	76 (7.8)	44	2	10	72
Zonguldak Bülent Ecevit University, Faculty of Medicine, Zonguldak	36 (3.7)	10	2	3	15
University of Health Sciences Antalya Training and Research Hospital, Antalya	34 (3.5)	117	3	1	16
Medical Faculty, Hacettepe University, Ankara	23 (2.4)	16	10	3	34
Osmangazi University, Faculty of Medicine, Zonguldak	15 (1.5)	44	2	10	72

Data in second column are number (%) of patients.

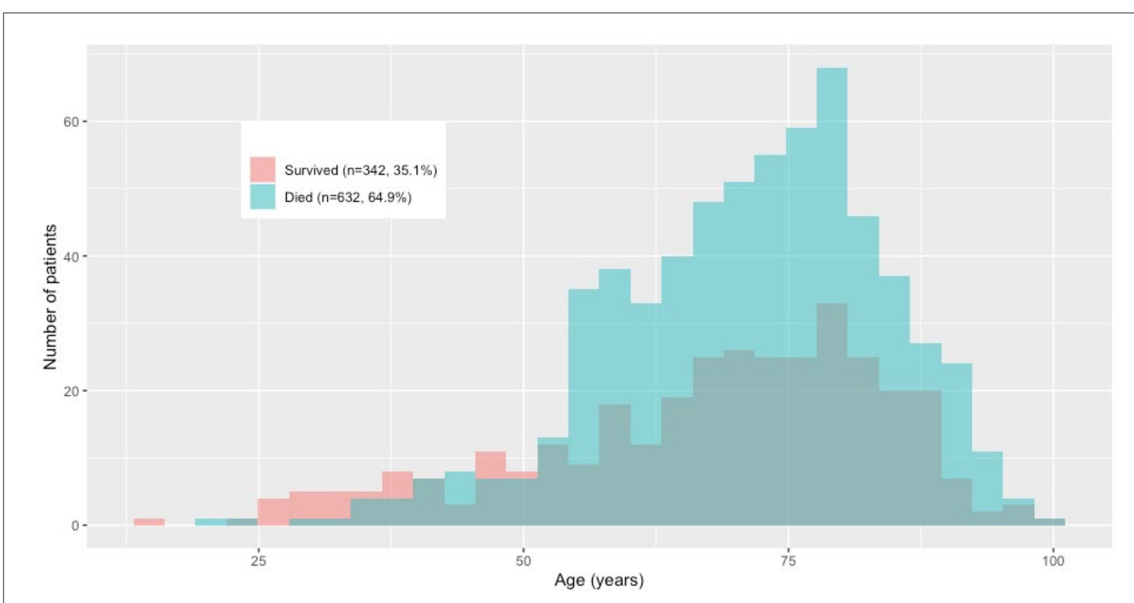

Figure 1. Age distribution of the study population by survival (n=974) (died vs survived, *P*=.01515, Wilcox on rank sum test with continuity correction).

isons between survivors and non-survivors. Results of the analysis were evaluated with 95% confidence interval, and P<.05 was accepted as a statistically significant difference.

RESULTS

During the study period, 974 patients were admitted to the ten ICUs (**Table 1**). Fifty-eight percent (n=571) were men. The median age and range was 75 (16-101) years for men and 69.5 (21-99) years for women (P<.001). The median and range age was 72 (21-101) years for patients who died (n=632, 64.9%)) and 70 (16-99) years for patients who lived (**Figure 1**, P<.001). The mean APACHE and SOFA scores were higher in patients who died than in surviving patients (P<.001, both comparisons). There was a travel history in 19 patients. The most common symptom was dyspnea followed by fever, cough, and headache (**Table 2**). Most patients were admitted to the emergency department (54.9%). The majority of patients admitted from the chest disease ward died (80.9%). Respiratory failure was the most common cause of hospitalization (82.5 %). Respiratory failure on admission was associated with death (P=.013).

The mean arterial pressure was higher in surviving patients (P=.004) (**Table 3**). Of laboratory values taken during admission, ferritin AST, ALT, and C reactive protein levels were significantly higher in patients who died. Most patients (n=719, 73.8%) underwent invasive mechanical ventilation therapy; 158 (22%) survived. Of the 211 patients who received noninvasive ventilation, 104 died (49.3%). Forty-six patients received oxygen with only a mask. Tidal volume and driving pressure were higher in patients who died (P=.010. and P=.008 respectively). Regarding the PaO_2/FiO_2 values during the ICU, most patients were classified with moderate to severe ARDS. Arterial blood gas values were signifi-

Table 2. Demographic and clinical characteristics (categorical variables).

	Survived (n=342)	Died (n=632)	*P*
Gender			
Female	150 (37.2)	253 (62.8)	.247
Male	192 (33.6)	379 (66.4)	
Symptoms	309 (34.6)	585 (65.4)	.230
Fever	126 (33.8)	247 (66.2)	.492
Dyspnea	277 (33.9)	541 (66.1)	.061
Coughing	151 (38.0)	246 (62.0)	.113
Headache	33 (28.7)	33 (28.7)	.125
Smoking	87 (33.6)	172 (66.4)	.549
Travel history	6 (31.6)	13 (68.4)	.744
Contact history	36 (32.4)	75 (67.6)	.530
Admission service			
Chest disease	9 (19.1)	38 (80.9)	
Infection	67 (26.6)	185 (73.4)	
Medical	13 (40.6)	19 (59.4)	.001
Emergency	215 (40.2)	320 (59.8)	
Other	38 (35.2)	70 (64.8)	
Reason for admission			
Respiratory failure	276 (34.3)	528 (65.7)	**.040**
Sepsis	8 (38.1)	13 (61.9)	

Table 2 (cont.). Demographic and clinical characteristics (categorical variables).

	Survived (n=342)	Died (n=632)	*P*
Other	40 (48.2)	43 (51.8)	**.040**
Multiple reason	18 (27.3)	48 (72.7)	
Admission respiratory failure	294 (33.8)	576 (66.2)	**.013**
Admission sepsis	23 (31.1)	51 (68.9)	.450
Admission other	43 (42.6)	58 (57.4)	.097
Diagnosis with PCR			
Negative	285 (38.6)	453 (61.4)	**<.001**
Positive	57 (24.2)	179 (75.8)	
Comorbidity	295 (33.4)	588 (66.6)	**.001**
Hypertension	173 (34.4)	330 (65.6)	.627
Diabetes	90 (33.0)	183 (67.0)	.381
Cardiac disease	127 (34.4)	242 (65.6)	.722
Pulmonary disease	107 (37.9)	175 (62.1)	.237
Malignity	53 (24.5)	163 (75.5)	**<.001**
Chronic renal failure	40 (33.6)	79 (66.4)	.715
Immune deficiency	22 (22.9)	74 (77.1)	**.008**

Data are number of patients (%).

Table 3. Clinical characteristics (continuous variables) by survival.

	Survived (n=342)	Died (n=632)	*P*
Age (years), median (range)	75.0 (16-101)	69.5 (21-99)	**<.001**
Body mass index (kg/m^2)	26.6 (17.3)	25.9 (13.5)	.507
Duration of symptoms before ICU (days)	3 (0-30)	2 (0-30)	.596
Apache II scores	23.5 (14.6)	29.7 (16.7)	**<.001**
SOFA scores	5.1 (2.6)	7.1 (3.3)	**<.001**
Length of ICU (days)	8 (1-96)	6 (1-78)	**<.001**
Length of invasive mechanical ventilation (days)	7 (1-66)	4 (1-170)	**.001**
Length of noninvasive mechanical ventilation (days)	3 (1-29)	3 (1-25)	.314
Fever (°C)	36.9 (0.8)	36.9 (0.8)	.844
Respiratory rate (/min)	24.6 (7.6)	25.3 (8.1)	.171
Heart rate (/min)	99.9 (20.9)	100.9 (21.9)	.490
Mean arterial pressure (mm Hg)	78.7 (21.0)	74.5 (22.1)	**.004**
SpO_2 (%)	91.3 (7.2)	89.7 (7.9)	**.002**
White blood cell (per mm^3)	9860 (960-108 000)	9820 (60-860 000)	.348
Lymphocyte (per mm^3)	1180 (100-25 300)	1000 (100-830 000)	.467
Platelet (per mm^3)	229 000 (203-4 333 000)	219 000 (300-331 0000)	.173
Neutrophil to lymphocyte ratio	7.3 (0.3-94)	10.3 (0.1-92.9)	**.004**
International normalized ratio	1.2 (0.8-13)	1.3 (0.9-138)	.314
Aspartate amino-transferase (U/L)	35 (6-1050)	45 (6-10 474)	**<.001**
Alanine amino-transferase (U/L)	24 (3-931)	29 (1-6428)	**.001**
D-dimer (ng/mL)	986 (0-36 146)	1848 (0.1-41 666)	.198
Creatinine (mg/dL)	1.1 (0.3-761)	1.5 (0.1-4223)	.337
Lactate (µg/L)	2 (0.1-797)	2.5 (0.1-4078)	.290
Ferritin (µg/L)	327 (9-4399)	553.7 (2-39 894)	**.002**
Fibrinogen (mg/dL)	524.8 (195.3)	549.8 (220.2)	.183
C-reactive protein (mg/L)	36.4 (0.1-450)	48 (0.1-498)	**.010**
Procalcitonin (ng/mL)	0.5 (0.1-12 680)	1.2 (0.1-21100)	.435
Echocardiography ejection fraction (%)	51.0 (13.4)	51.6 (12.2)	.806

cantly lower in the patients who lived than died (**Table 3**). The neutrophil-to-lymphocyte ratio was higher than normal in all patients at admission, but was higher in patients who died than in those who survived (*P*=.004).

All 974 patients were tested by TR-PCR; 236 (22.4%) were positive; 236 patients were diagnosed by RT-PCR, 138 were patients diagnosed as COVID-19 positive by clinical-radiology had negative RT-PCR results. Chest radiography was not available in 259 patients during hospitalization. Chest radiography revealed pathology in 539/715 patients at the time of admission. Bilateral infiltrates were detected on radiography in 556/715 patients. Chest radiography results were significantly higher in patients who died than in those who survived. At admission, 884 patients underwent computed tomography (CT). Eighty-six percent (767/884) of these patients had bilateral ground-glass opacification on CT scan. There were no significant differences in CT imaging between the patients who lived and died (**Table 4**).

One or more comorbidities were detected in 883/974 of the patients. Hypertension, cardiac disease, diabetes mellitus, chronic kidney disease, chronic lung disease, malignancy, and immune deficiency were the most common comorbidities. The presence of malignancy and immunodeficiency was statistically higher in patients who died (*P*<.001 and *P*=.008, respectively) (**Table 2**). Ventricular fibrillation/tachycardia (VF/VT) occurred in 7.9% in all the patients, while the mortality rate was 81.8% in patients with VF/VT, it was 63.4% in those who did not (*P*=.001).

The prone position was applied to 19% of patients. While 55.7% of the patients who were in the prone position died, the mortality rate was 67% in the patients not applied (*P*=.004). Hydroxychloroquine sulfate (Plaquenil/generic) was given to 809 patients, 816 patients received antivirals Enfluvir (oseltamivir), Kaletra (50 mg ritonavir and 200 mg lopinavir), Favipiravir (favipiravir), and 918 received antibiotic therapy. Cytokine removal was performed in 17 patients undergoing renal replacement therapy. Tocilizumab, a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R) was administered to 71 patients. More patients who underwent renal replacement therapy, or used hydroxychloroquine, antivirals, and vasopressors died than lived (*P*<.001) (**Table 4**). The rate of steroid use in all the patients was 15%. Organ failure was present in 33.5% of patients. In terms of organ failure, ARDS, renal failure, and sepsis were significantly higher in patients who died than in those who survived (*P*<.001) (**Table 5**). The duration of invasive mechanical ventilation and ICU stay was significantly longer in those who survived (*P*<.001) (**Table 5**).

DISCUSSION

Data on Turkish COVID-19 patients in intensive care has been limited to small groups of patients, including our previous study.[5] In this report, we summarize data on patients diagnosed with COVID-19 in ten ICUs in Turkey from 15 March to 30 June 2020. Of 974 patients, 632 died (64.9%). By comparison, in a study of 2215 patients admitted to ICUs at 65 hospitals from March 4 to April 4, 2020 in the United States,[10] 35.4% died within 28 days. In a cohort of 1500 critically ill ICU patients with COVID-19 in Lombardy, Italy,[11] the ICU mortality was 26%. In a study in Wuhan, China in January 2020, the mortality rate was 4.3% in 36 of 138 patients with COVID-19 admitted to the ICU.[12] The median age of the ICU patients was older than non-ICU patients in the Wuhan study (66 years vs 51 years) and the ICU patients had more comorbidities. In our study, most of the patients were admitted to the ICU because of respiratory failure. The majority of patients were hospitalized directly from the emergency room to the ICU. The median age in our study was 72 years.

In the US study, the most common symptoms before ICU admission were cough (77.1%), dyspnea (74.9%), and fever (70.7%). A total of 1738 patients had at least one comorbidity, such as hypertension, diabetes, and chronic lung disease. 1738 patients (78.5%) had at least 1 comorbidities, including hypertension (59.7%), diabetes (38.9%), and chronic lung disease (24.0%). As in our study, the most common symptoms were cough and dyspnea in the US and Italy studies as in our study.[10,11] In our study, the most common comorbidities were cardiovascular disease and hypertension and high APACHE II and SOFA scores, which is consistent with other studies.[12,13]

In a European multicenter study of 4244 critically ill adults with COVID-19, high-flow oxygen, standard oxygen therapy, and non-invasive ventilation were applied to patients at the time of ICU admission, from February 25 to May 4, 2020.[13] Sixty-three percent of the patients were intubated during the first 24 hours while 3376 (80%) established invasive mechanical ventilation during their ICU stay. The median plateau pressures and PEEP were 24 cmH_2O and 12 cmH_2O, respectively. The median PaO_2:FIO_2 ratio was 154 mm Hg during the first 24 hours. Gupta et al[10] reported that 1494 patients (67.4%) received invasive mechanical ventilator support, and 958 (48.3%) received vasopressors on the day of ICU admission in their study. The median PaO_2:FIO_2 ratio was 124 mmHg (IQR, 86-188 mmHg). In another Italian study, 1300 patients received ventilator support, 11% of whom received noninvasive ventilation and 88% of whom received invasive mechanical ventilation.[11]

Table 3 (cont.). Clinical characteristics (continuous variables).

	Survived (n=342)	Died (n=632)	*P*
FiO_2	42.1 (27.3)	40.8 (31.8)	.529
PEEP (cmH_2O)	7.5 (2.2)	7.7 (2.1)	.145
Tidal volume (mL)	460.9 (66.8)	475.8 (64.1)	**.010**
P_{Peak}	24.2 (4.9)	25.9 (23.1)	.352
$P_{Plateau}$	19.5 (5.3)	20.4 (4.8)	.071
Compliance (mL cm H_2O)	36.3 (13.6)	34.8 (10.9)	.293
Driving pressure	12.1 (4.4)	13.4 (4.4)	**.008**
PaO_2 FiO_2 ratio	198.4 (104.8)	165.7 (93.5)	**<.001**
Highest PEEP (cmH_20)	8.8 (3.5)	9.6 (4.0)	.035
Lowest PEEP (cmH_20)	6.7 (6.2)	6.7 (2.7)	.971
Max PaO_2FiO_2 ratio	297.3 (199.7)	225.9 (146.5)	**<.001**
Min PaO_2FiO_2 ratio	158.6 (79.0)	130.3 (69.0)	**<.001**
Max PaO_2	105.6 (68.8)	92.4 (68.2)	**.005**
Min PaO_2	59.7 (58.9)	51.5 (35.8)	**.009**
Max P_{Peak}	27.4 (11.3)	28.4 (7.7)	.154
Min P_{Peak}	21.2 (4.6)	22.0 (5.1)	.069
Compliance (max)	40.2 (13.6)	37.9 (11.5)	.067
Compliance (min)	30.9 (11.3)	29.2 (10.2)	.113

Values are mean (standard deviation) unless noted otherwise. PEEP: positive end-expiratory pressure.

The median PEEP, maximum PEEP, and PaO_2/FIO_2 were 14 cmH_2O, 22 cmH_2O, and 160, respectively. In our study invasive mechanical ventilation was required in 74% and 21% of the patients, respectively. The median PEEP, maximum PEEP, and PaO_2/FIO_2 values, which is consistent with other studies.[10-12]

Clinical findings should be evaluated using laboratory and radiological findings for the diagnosis of COVID-19. Fang et al[14] reported that the sensitivity of chest CT was greater than that of RT-PCR (98% vs. 71%, respectively, *P*<.001) for the diagnosis of COVID 19. They concluded that the use of chest CT is preferred for screening for COVD-19 particularly when RT-PCR testing is negative. The reasons for the low efficiency of viral nucleic acid detection might be due to the immature development of nucleic acid detection technology, low patient viral load, improper clinical sampling technique, location of collection, time of onset of symptoms, storage and transportation of the sample to the location of the examination, and variation in detection rate from different manufacturers. Floriano et alreported on the accuracy of the PCR test in ARDS due to COVID-19 in a systematic review and meta-analysis.[15] When disease prevalence was low, PCR was accurate in 55% of the cases. The sensitivity of the RT-PCR test varied from 45% and 67%.[16] Due to the low sensitivity and specificity of the COVID-19 laboratory test, patients diagnosed clinically and radiologically were included in this study.

In the COVID-19 pandemic, the function of imaging has grown rapidly. Due to its availability, low cost, and ease of use compared with CT, chest radiography is routinely performed at the time of admission. In early mechanical ventilation among COVID-19 patients, more opacities are associated with several fold increases on chest radiography.[17] In other words, more opacities on chest radiography are associated with higher rates of early intubation within 48 h of admission among COVID-19 patients. We have also detected more pathology on chest radiography in patients who died. CT imaging of COVID-19 is non-specific, but it has specific characteristics that are used to diagnose the disease by experienced radiologists. These findings are comparable to those of other viral pneumonias, but the symptoms are quite typical. Ground-glass opacity is the most common and earliest pattern, which may be unifocal at first, but typically bilateral, multifocal, with predominantly peripheral distribution, especially in the lower lobes.[18] In our study, most of the patients had bilateral ground glass opacification on CT scan, which is consistent with other studies.

Currently, there are no proven and effective treatments for COVID-19. Remdesivir, favipiravir, hydroxychloroquine, azithromycin, lopinavir/ritonavir, nafamostat mesylate, and others have been used for COVID-19 disease. Despite intensive research effort, as shown by more than 600 clinical trials currently underway, no effective drugs have been approved to cure COVID-19 and compassionate treatment is the only standard therapy.[19] The Randomized Study of COVID-19 Therapy (RECOVERY) is a large clinical trial of different therapies for individuals admitted to hospitals with serious COVID-19 infection.[20] As of December 2020, nine strategies for the treatment of adults were evaluated

Table 4. Radiologic findings and therapies.

	Survived (n=342)	Died (n=632)	*P*
Radiography	258/715 (36.1)	457 (63.9)	.292
Pathology	329 (61.5)	206 (38.5)	**.020**
Bilateral infiltrates	197 (35.5)	358 (64.5)	.542
Pleural effusion	75 (41.0)	108 (59.0)	.110
Irregular opacities	117 (35.9)	209 (64.1)	.921
Computerized tomography	311 (35.2)	573 (64.8)	.889
CT bilateral ground-glass opacification	262 (34.4)	499 (65.6)	.244
CT pleural effusion	133 (35.6)	241 (64.4)	.839
CT nodules	77 (33.6)	152 (66.4)	.567
Cardiac arrest	22 (16.3)	113 (83.7)	<.001
VT/VF	14 (18.2)	63 (81.8)	.001
Recruitment	51 (29.1)	124 (70.9)	.068
Prone position	82 (44.3)	103 (55.7)	.004
Renal replacement	55 (24.2)	172 (75.8)	<.001
Convalescent plasma	13 (23.2)	43 (76.8)	.055
Hydroxychloroquine	269 (33.3)	540 (66.7)	.007
Antibiotic	316 (34.4)	602 (65.6)	.068
Antiviral	264 (32.4)	552 (67.6)	**<.001**
Vasopressor	87 (15.2)	488 (84.9)	**<.001**
Tocilizumab	20 (28.2)	51 (71.8)	.203
Cytokine removal	6 (35.3)	11 (64.7)	.987

Data are number of patients (%).

Table 5. Organ failure and antibiotic culture results.

	Survived (n=342)	Died (n=632)	*P*
Organ failure			
No	190 (58.3)	136 (41.7)	**<.001**
ARDS	73 (27.9)	189 (72.1)	
Renal failure	13 (35.1)	24 (64.9)	
Sepsis	24 (22.9)	81 (77.1)	
Liver failure	2 (66.7)	1 (33.3)	
DIC	0 (-)	1 (100.0)	
Multiple organ failure	40 (16.7)	200 (83.3)	
Adult respiratory distress syndrome	109 (24.5)	336 (75.5)	**<.001**
Renal failure	25 (16.9)	123 (83.1)	**<.001**
Sepsis	59 (18.4)	262 (81.6)	**<.001**
Liver failure	3 (17.6)	14 (82.4)	.128
Disseminated intravascular coagulation	0 (-)	3 (100.0)	-
Culture positive	57 (30.8)	128 (69.2)	.173

in the trial: seven repurposed drugs, one newly created drug, and convalescent plasma. Dexamethasone improved the survival of patients receiving invasive mechanical ventilation or oxygen at randomization. In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%). Since there was not enough evidence to support the use of steroids at the beginning of the pandemic, we did not routinely use steroids in our patients. Recommendations on this subject began to be published in early 2021.[20] We found that the rate of steroid use in all patients was 15%. This may help explain the higher mortality rate in our study.

Fifty-two critically ill adult patients with COVID-19 pneumonia were admitted to the ICU in the study by Yang et al.[21] The mean age of the patients was 59.7 years, 35 (67%) were men, 21 (40%) had chronic illness, and 98% of the patients had fever. Thirty-two (61.5%) died after twenty-eight days. APACHE and SOFA scores were higher in patients who died than in surviving patients. Patients who died were older than survivors (64.6 years vs 51.9 years). Seventy-one percent of patients required mechanical ventilation. Most patients had organ function damage, including ARDS (67%), acute kidney injury (29%), cardiac injury (23%), and hepatic dysfunction (29%). In our study, the rate of male patients was higher than that reported by Yang et al. Our patients were older than their patients and had a very high rate of comorbidities. The APACHE and SOFA scores in our study patients were much higher than those in the study by Yang et al. Therefore, the mortality rate in our study may have been higher than that in that study.

To maximize the use of ICU treatment and other hospital services, it is important to recognize the determinants of the outcomes of critically ill patients with extreme COVID-19. In a European multicenter study,[13] the 90-day mortality was separately correlated with older age, obesity, diabetes, immunocompromised status, lower PaO_2/FIO_2 ratio, and greater hemodynamic and renal SOFA scores at ICU admission. These findings highlight the effect of premorbid conditions and multi-organ damage on the outcomes of patients in the COVID-19. The European multicentric study showed that the overall 90-day mortality was 31% and was higher in older and immunocompromised patients, obese patients, diabetics, and those who had multiple organ dysfunction upon ICU admission.[13] The investigators reported that patient age, invasive ventilation rate, hypertension frequency, and immune deficiency frequency were 63% (57-71) years and 63%, 48%, and 7%, respectively. The SOFA score was 5 for all patients. Our patients were older than the patients in the European multicenter study. In addition, the rates of comorbidities such as hypertension and immunocompromised patients were higher. The invasive ventilation management rate was also higher in our study (74% vs. 63%). We found a SOFA score of 6.4 (3.2) in all patients. The mortality rate was 64.9% in our study and in older patients, and the presence of malignancy and immunodeficiency was statistically higher in patients who died.

Recently, in a systematic review and meta-analysis of 52 studies involving 43 128 patients, the ICU mortality rate was 35.5% (95% CI 31.3%-39.9%, and varied from 0 to 84.6%.[22] Hospital mortality rates significantly and progressively declined in the UK during the first wave of the pandemic between March and August, 2020 in patients with COVID-19.[23] Hospital mortality was higher in the period from March 9 to April 26, 2020, than in the period from June 15 to August 2, 2020. They reported that most patients in the first wave were older (i.e., median age 70 years), had two or more comorbidities, and were of white ethnicity, and hospital mortality was highest in these groups. Mortality reduction may be explained by changes in breathing and lung-related support and steroid treatment, together with changes in other organ support management. In addition, this wide range of mortality rates may be related to the mean age of patients hospitalized in the ICU, comorbidity, critical care capacity strain, and the reliability of reported research.

Our study has several limitations. First, it was a retrospective study based on data mainly recorded from hospital database systems. Although the Turkish Ministry of Health made recommendations for the treatment of COVID-19 patients, ICU admission policies and patient management may not have been identical in all centers. COVID-19 is a challenge for ICUs and healthcare systems worldwide. In 974 critically ill patients with COVID-19 admitted to ICUs, the mortality rate was high (64.9%) in this multicenter study. The majority of patients needed respiratory support after diagnosis of COVID-19.

Author contributions

HS writing the original draft, review and editing, UA, CÖ, conceptualization, data collection, formal analysis, investigation, methodology. KTS, VY, AS, AZT, AAA, HA, NKÖ, NDB, BY, EB, GK, DA, PD, FC, AÇ, SK data collection.

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